Memory in Induced Pluripotent Stem Cells: Reprogrammed Human Retinal Pigmented Epithelial Cells Show Tendency for Spontaneous Redifferentiation.

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Public Summary:
Induced pluripotent stem (iPS) cells have been generated from a variety of somatic cell types via introduction of transcription factors that mediate pluripotency. However, it is unknown that all cell types can be reprogrammed, and whether the origin of the parental cell ultimately determines the behavior of the resultant iPS cell line. We sought to determine whether human retinal pigmented epithelial (RPE) cells could be reprogrammed, and to test the hypothesis that reprogrammed cells retain a "memory" of their origin in terms of propensity for differentiation. We reprogrammed primary fetal RPE cells via lentiviral expression of OCT4, SOX2, LIN28, and Nanog. The iPS cell lines derived from RPE exhibited morphologies similar to human embryonic stem cells and other iPS cell lines, expressed stem cell markers, and formed teratomas containing derivatives of all three germ layers. To test whether these iPS cells retained epigenetic imprints from the parental RPE cells, we analyzed their propensity for spontaneous differentiation back into RPE after removal of FGF2. We found that some, but not all, iPS lines exhibited a marked preference for redifferentiation into RPE. Our results show that RPE cells can be reprogrammed to pluripotency, and suggest that they often retain a memory of their previous state of differentiation.

Scientific Abstract:
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